## FROM RESEARCH TO PRACTICE



## Practical Aspects and Exercise Safety Benefits of Automated Insulin Delivery Systems in Type 1 Diabetes

Dessi P. Zaharieva,<sup>1</sup> Dale Morrison,<sup>2</sup> Barbora Paldus,<sup>2,3</sup> Rayhan A. Lal,<sup>1,4,5</sup> Bruce A. Buckingham,<sup>1,4</sup> and David N. O'Neal<sup>2,3</sup>

<sup>1</sup> Division of Endocrinology, Department of Pediatrics, Stanford University School of Medicine, Stanford, CA; <sup>2</sup> Department of Medicine, The University of Melbourne, Melbourne, Australia; <sup>3</sup> Department of Endocrinology & Diabetes, St Vincent's Hospital Melbourne, Melbourne, Australia; <sup>4</sup> Stanford Diabetes Research Center, Stanford, CA; <sup>5</sup> Division of Endocrinology, Department of Medicine, Stanford University School of Medicine, Stanford, CA

Regular exercise is essential to overall cardiovascular health and well-being in people with type 1 diabetes, but exercise can also lead to increased glycemic disturbances. Automated insulin delivery (AID) technology has been shown to modestly improve glycemic time in range (TIR) in adults with type 1 diabetes and significantly improve TIR in youth with type 1 diabetes. Available AID systems still require some user-initiated changes to the settings and, in some cases, significant pre-planning for exercise. Many exercise recommendations for type 1 diabetes were developed initially for people using multiple daily insulin injections or insulin pump therapy. This article highlights recommendations and practical strategies for using AID around exercise in type 1 diabetes.

For individuals with type I diabetes, exercise and physical activity can lead to disturbances in glycemia, particularly in the absence of preparation and implementation of preventative strategies to minimize hypoglycemia risk such as insulin dose adjustments and/or carbohydrate feeding. Automated insulin delivery (AID) systems have been shown to improve overall glycemia, specifically increasing time in range (TIR; time spent with glucose levels between 70 and 180 mg/dL) and reducing hypoglycemia (glucose <70 mg/dL) for youth and adults with type I diabetes (1-4). A recent systematic review and meta-analysis demonstrated that AID systems also moderately improve TIR during exercise and physical activity compared with standard of care (I). With AID technology, advanced algorithms and automation of insulin dosing can remove some of the guesswork around daily glycemic management. However, exercise and regular physical activity continue to challenge the accuracy of continuous glucose monitoring (CGM) systems and the ability for AID systems to maintain glucose levels in the target range. This obstacle is, in part, the result of the variable physiological responses associated with differing types, intensities, and durations of exercise, combined with the individual variance in response to activity. Conversely, each commercially available AID system has slightly different functionality and features that, in turn, require individualized approaches to prepare for exercise. This article summarizes the practical uses of AID technology and

its safety benefits during and after exercise for youth and adults with type I diabetes.

# Exercise and the Pharmacological Limitations of Rapid- and Ultra-Rapid-Acting Insulins

During exercise in people without diabetes, insulin secretion drops rapidly to facilitate glucose release from the liver to match the rate of glucose uptake into the working muscles. However, for individuals with type I diabetes who are undertaking exercise, plasma insulin concentration cannot be decreased rapidly at the start of exercise and might even rise in the systemic circulation (5). Indeed, it has been demonstrated that rapid reductions in insulin delivery provided by AID algorithms in response to declining blood glucose levels with exercise do not correspond to equally rapid changes in circulating free insulin levels (6).

This pharmacodynamic limitation of subcutaneous delivery of rapid-acting insulins, characterized by a delayed onset and offset of action (7,8), limits the ability of AID systems to address the rapid changes in insulin requirements associated with exercise. Faster-acting insulin aspart (FiAsp), an ultra-rapid-acting insulin recently approved for use in some AID systems, has a more rapid onset and a shorter duration of insulin action (9) than insulin aspart. However, this difference is not of a sufficient magnitude to meaningfully affect residual insulin action during exercise. A recent study demonstrated no



Corresponding author: Dessi P. Zaharieva, dessi@stanford.edu https://doi.org/10.2337/dsi22-0018

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clinically meaningful benefit in glucose control during or in the 24 hours after exercise with FiAsp compared with insulin aspart used in conjunction with the Medtronic MiniMed 78oG AID system (10). A sufficiently responsive insulin with a rapid onset and short duration of action could address this obstacle to glucose control in people with type I diabetes who use AID. However, no such formulation currently exists. In fact, complete restoration of the physiological responsiveness of insulin action may not be feasible when insulin is administered subcutaneously and not directly into the portal circulation.

Importantly, the currently recommended strategies for using AID systems to minimize hypoglycemia during and after exercise relate to the need to minimize the insulin on board (IOB; active insulin in the body) during times of heightened insulin sensitivity induced by exercise and associated contraction-mediated glucose uptake. In situations when IOB cannot be minimized before or after exercise, carbohydrate supplementation is often required to offset the increased glucose usage in peripheral tissues.

#### **AID Strategies for Exercise**

Commercially available AID systems still require some user interaction and, therefore, are sometimes referred to as hybrid closed-loop systems and not fully automated closed-loop systems. With AID technology, user-initiated modifications to insulin pump settings may be necessary for exercise. For optimal use, certain AID strategies for exercise involve significant pre-planning (e.g., setting an exercise

target), while other strategies that can be implemented at the time of exercise onset (e.g., pump suspension) may limit this requirement for pre-planning. Planning for exercise cannot only minimize IOB, but, when it includes setting a higher glucose target, may also reduce the need for supplemental carbohydrate intake before exercise, which is important for individuals who may be focused on weight loss, for example. Table I summarizes various AID strategies for planned and unplanned/spontaneous exercise.

## Important Considerations for AID and Exercise

Setting Elevated AID Glucose Targets for Exercise

Exercise consensus guidelines and position statements commonly mention significant pre-planning as a strategy to reduce the risk of exercise-associated hypoglycemia during exercise (II-I3). Guidelines and evidence-based research have shown that setting a higher exercise glucose target starting I-2 hours before exercise until the end of exercise if the activity is  $\geq$ 30 minutes in duration is an effective strategy to reduce the risk of hypoglycemia during exercise (II-I3). Activities that are shorter in duration (i.e., <30 minutes) may not require setting a higher exercise target; however, additional research is needed in this area. To address the potential risk of delayed hypoglycemia after exercise, it may be recommended to extend the exercise target for I-2 hours into post-exercise recovery and/or overnight, analogous to the application of a temporary basal rate reduction in open-loop conditions (14,15).

 TABLE 1
 AID Strategies to Decrease IOB and/or Maintain Glucose Levels for Planned and Unplanned/Spontaneous Exercise

Strategy	Description
Strategies for planned exercise	
Combination strategy	Set exercise target before onset of exercise (optimally 1–2 hours in advance) and reduce mealtime bolus insulin 1–3 hours before exercise.*
Set exercise target	Set exercise target before onset of exercise (optimally 1-2 hours in advance).
Reduce mealtime bolus insulin	Reduce mealtime bolus insulin 1-3 hours before exercise.*
Use manual mode and temp basal settings	Exit automated mode and use manual mode with recommended 50-80% basal insulin reduction set 90 minutes before exercise; may require additional carbohydrate feeding before exercise.
Check blood glucose	Perform fingerstick blood glucose check† and/or check CGM trend arrows and determine a plan of action for exercise.
Check IOB	Check IOB and determine a plan of action for exercise.
Strategies for unplanned/spontaneous exerci	ise
Carbohydrate feeding	Eat carbohydrates at exercise onset or during exercise.‡
Insulin pump suspension	Suspend insulin delivery at exercise onset and resume it at the end of exercise.
No change	Leave usual AID settings with no changes for exercise.

<sup>\*</sup>If exercise is likely to occur 1-3 hours after a meal, a reduction in the mealtime bolus may be compensated by increased insulin delivery by the AID system, still resulting in increased IOB during exercise. †Fingerstick blood glucose checks may not be needed before exercise but may be suitable during rapid changes in glucose during exercise because of the potential increase in CGM lag time (29,31). ‡Additional carbohydrate feeding may be required during unplanned/spontaneous exercise, particularly in situations with higher IOB.

People with type I diabetes who more commonly experience a rise in glycemia during or after exercise because of counterregulatory hormone responses that overcompensate for glucose utilization (e.g., in the context of morning, fasted, high-intensity, or resistance exercise) may wish to consider avoiding the use of a higher exercise target in advance of the activity. For these specific cases, the more prudent recommendation is to leave the glucose target on the AID system unchanged, because setting a higher glucose target may lead to significant hyperglycemia. However, this strategy is dependent on the specific AID system being used and also currently lacks research evidence. Therefore, this recommendation is made with caution.

#### Practical Tips Regarding Elevated AID Targets for Exercise

It may be helpful for diabetes care providers and diabetes educators to provide patients with additional resources and guidance on strategies for setting exercise targets (16). Individuals with type I diabetes who are unsure about their typical blood glucose responses to exercise may benefit from additional information about more accurately determining exercise intensity. Exercise consensus guidelines (12,13) demonstrate that aerobic exercise (e.g., walking, jogging, and cycling) may lead to a drop in glycemia, whereas some anaerobic exercise (e.g., sprinting and power-lifting) may lead to a rise in glycemia for individuals with type I diabetes. However, determining the exact exercise intensity may be difficult for some individuals.

In such cases, a useful strategy is to advise patients not to focus on achieving a target heart rate during exercise, but rather to focus on their perception of the intensity (i.e., how the activity makes them feel). For example, it may be helpful to provide patients with a modified Borg scale of perceived exertion (17–19) of 0–10 and explain where aerobic and anaerobic activities typically fall on that scale (Table 2). A modified Borg scale may include rating definitions of 0 = no activity, I = very light activity, 2–3 = light activity, 4–6 = moderate activity, 7–8 = vigorous activity, 9 = very hard activity, and IO = maximal-effort activity. Generally, aerobic activities may fall in the 2–8 range on the modified

Borg scale, and anaerobic activities are more likely to fall in the 7–10 range, although there is some flexibility around the exact numbers. The practical benefit of patients more accurately determining their exercise intensity is that they will recognize situations in which they will need to set a higher glucose target on their AID system (e.g., for moderate-intensity or prolonged aerobic exercise in the 2–8 range on the Borg scale), as well as situations in which setting a higher target may not be necessary (e.g., vigorous-intensity or high-intensity interval training in the morning or short bouts of exercise in the 7–10 range on the Borg scale). We encourage people with type I diabetes to review their CGM data at the start, during, and after exercise to gain insights into the aforementioned strategy.

Another important tip is to understand that, depending on the AID system being used, the glucose level, and the glucose rate of change, setting a higher exercise target with AID generally alters basal insulin delivery but may or may not stop the AID system from initiating automated bolus delivery (Table 3). Similarities and differences for exercise among the available AID systems are described in more detail in Table 3. Commercial AID systems are often not transparent with regard to their algorithm design, so we present what is known based on limited marketing data. In contrast, open-source AID systems feature algorithm transparency and are designed for flexibility in user customizations (20). With the MiniMed 780G system, the exercise target (called Temp Target) decreases insulin delivery, disables the automated bolus feature, and raises the glucose target to 150 mg/dL. Of importance, the automated bolus correction feature will not resume until the exercise target is ceased. With the Omnipod 5 system, the exercise target (called Activity) decreases insulin delivery by  $\sim$ 50% and increases the glucose target to 150 mg/dL. In addition, insulin delivery is constrained by the increasing calculations of IOB. With the Control-IQ system, the exercise target (called Exercise) uses a treatment range of 140-160 mg/dL. This means that Control-IO will decrease basal insulin when glucose is predicted to be <140 mg/dL

TABLE 2   Example of a	Modified Borg Scale
Rating	Description
0	No activity: sitting or lying down, no change to breathing
1	Very, very light activity: breathing relatively unchanged
2-3	Light activity: easy to breathe, can carry on a conversation
4-6	Moderate activity: breathing more heavily, can carry on conversation but requires more effort
7-8	Vigorous activity: breathing is slightly uncomfortable, carrying on conversation requires maximal effort
9	Very, very hard activity: difficultly maintaining exercise or carrying on a conversation
10	Maximal effort activity: full-out effort, no conversation possible

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AID System	Sensor and Pump Technology	Standard Glucose Target, mg/dL	Exercise Glucose Target, mg/dL	Exercise Target Terminology	Additional Information
MiniMed 670G/770G (Medtronic)	Guardian Sensor 3 CGM sensor and 670G or 770G insulin pump	120	150	Temp Target	Program for duration of time; will automatically deactivate at the end of the programmed time period
MiniMed 780G (Medtronic)	Guardian Sensor 4 CGM sensor and 780G insulin pump	100, 110, or 120	150	Temp Target	Program for duration of time; will automatically deactivate at end of the programmed time period; Temp Target disables the automated bolus feature
Control-IQ (Tandem)	Dexcom G6 CGM sensor and t:slim X2 insulin pump	112-160	140-160	Exercise Activity (up to six personal profiles can be created with personalized basal doses, insulin-to-carbohydrate ratios, and insulin sensitivity factors for use with Exercise Activity)	Manual start/stop—cannot program a duration of time; exercise mode suspends insulin delivery at a higher predicted glucose than standard mode but delivers insulin for usual hyperglycemic targets; overrides programmed sleep mode unless exercise mode switched off
CamAPS FX (CamDiab)	Dexcom G6 CGM sensor and Dana RS or Dana-i insulin pump	105 (customizable)	Customizable	Ease-Off or Planned Ease-Off	Program for duration of time; will automatically deactivate at the end of the programmed time period
Omnipod 5 (Insulet)	Dexcom G6 CGM sensor and Omnipod Pod insulin pump	110, 120, 130, 140, or 150 (customizable throughout the day)	150	Activity	During activity feature, automated insulin delivery is decreased, calculated IOB is increased, and maximum insulin delivery is restricted; enable for 1-24 hours; will automatically deactivate at end of enabled time period
OpenAPS algorithm (OpenAPS, AndroidAPS, FreeAPS X)	Variety of systems	Customizable	Customizable	Ability to change/scale all insulin delivery parameters (aggressiveness of automation) and targets	Program for duration of time or schedule for specific time; will automatically deactivate at the end of the programmed or scheduled time period
Loop algorithm (Loop, FreeAPS)	Variety of systems	Customizable	Customizable	Ability to change/scale all insulin delivery parameters (aggressiveness of automation) and targets	Program for duration of time or schedule for specific time; will automatically deactivate at the end of the programmed or scheduled time period

TABLE 3 Exercise	FABLE 3         Exercise Targets and Settings for Available	ole AID Systems			
AID System	Sensor and Pump Technology	Standard Glucose Target, mg/dL	Exercise Glucose Target, mg/dL	Exercise Target Terminology	Additional Information
Insulin-only bionic pancreas (Beta Bionics)	Dexcom G6 CGM and iLet bionic pancreas	Usually 120; can be changed by ±10	Can increase target to 130	No specific feature	Target is changed manually; no automatic deactivation

Updated and modified from refs. 13 and 16. \*Received CE-marked approval in the European Union and United Kingdom and approval in Canada, Australia, and New Zealand. †Received CE-marked approval in the European Union and United Kingdom; only commercially available in Europe. ‡Received U.S. Food and Drug Administration clearance; only commercially available in the United States. APS, artificial pancreas system. 30 minutes in the future and increase basal insulin when glucose is predicted to be >160 mg/dL 30 minutes in the future so the usual upper target is maintained. With the CamAPS FX system, there is a function (called Ease-Off) that is used to substantially reduce basal insulin delivery and temporarily raise the glucose target. This system has an additional option to pre-program Ease-Off if users know that exercise will occur at a specific time of day.

# User-Determined Insulin Dose Adjustments for Exercise With AID

Given that commercially available AID systems use hybrid closed-loop technology (i.e., they are not fully automated), manual insulin dosing by users is still required. However, to date, limited research evidence exists around the optimal dose adjustments that should be applied before and after exercise. Current guidelines follow similar strategies for both open-loop and AID systems. For preexercise dosing, the recommendation is to limit bolus IOB such that, ideally, exercise would be performed >3 hours after the preceding meal bolus. When such a significant level of pre-planning is not possible (e.g., if activity is going to occur 1-3 hours after a meal), the recommendation is to reduce bolus insulin by 25-75% (21). However, there is a caveat that AID systems may give extra insulin to make up the difference if glucose levels become elevated, so IOB at the onset of exercise may still be higher than desired. Overall, more specific research is needed in this area to optimize the timing and amount of bolus insulin reductions with AID systems around exercise.

For post-exercise adjustments, in general, exercise leads to increased insulin sensitivity for at least 7-II hours after exercise (22); therefore, also applying these bolus reduction strategies with the meal after exercise may be recommended. However, the increase in insulin sensitivity is dependent on the mode and characteristics of the exercise performed. Specifically, increases in insulin sensitivity after exercise are proportional to the intensity of exercise performed. Recent evidence demonstrates that vigorous resistance exercise that occurs in the evening increases hypoglycemia risk after the evening meal (39 vs. 14% for resistance exercise vs. control), whereas moderate-intensity exercise does not (10 vs. 14%) (23). Thus, a reduction in the post-exercise meal bolus may be more strongly recommended for vigorous resistance exercise; however, further evidence is needed to determine optimal insulin dosing adjustments after exercise across a spectrum of exercise modes (e.g., morning vs. evening and moderate-intensity vs. high-intensity exercise).

### Practical Tips for Insulin Dose Adjustments Around Exercise With AID

Open-source AID systems allow initiation of temporary profiles and override presets that can temporarily reduce the aggressiveness of the carbohydrate-to-insulin ratio, which allows for accurate recording of carbohydrates (II). The Control-IQ, MiniMed 780G, and Omnipod 5 systems do not allow users to make a direct reduction to mealtime bolus insulin delivery. Therefore, a more common strategy with these systems is to enter fewer carbohydrates than those actually being consumed to allow the system to recommend a reduced bolus insulin amount. With the CamAPS FX system, after users enter the carbohydrate amount and see the suggested bolus amount, they are able to tap on the bolus amount and change the dose (e.g., to half the dose). As discussed above, there is a caveat with AID systems that resulting hyperglycemia may trigger additional automated insulin delivery, which could occur later after the meal. If done before exercise, this could cause increased IOB at the time of exercise. With the Control-IQ system, an option for individuals with type I diabetes to reduce their mealtime bolus insulin would be to give a dual-wave bolus and then stop the extended bolus.

In most cases, AID systems manage post-exercise glycemia well overnight (23). However, in some cases, if individuals with type I diabetes experience recurrent nocturnal hypoglycemia after exercise, setting an exercise target at bedtime may be a consideration to help increase glucose concentrations. For example, with the MiniMed 78oG and the Omnipod 5 systems, exercise targets can be set for a user-specified duration at bedtime. With Control IQ, currently there is no similar option (i.e., the exercise target must be manually turned off), so this may not be a preferred strategy at bedtime. With the CamAPS FX system, users can set the Ease-Off feature at bedtime for a duration of time (from 0 to 24 hours). Research evidence is still needed to determine the optimal duration and timing of exercise targets overnight.

## Carbohydrate Supplementation to Prevent Hypoglycemia During Exercise With AID

Although setting exercise targets and reducing basal insulin (with open-loop pumps or multiple daily injections) well in advance of exercise are effective strategies to reduce hypoglycemia (23–25), they require a significant level of forward planning and not surprisingly have recently been shown to be among the least-used strategies (26). Therefore, additional practical recommendations are needed for situations in which individuals with type I diabetes cannot pre-plan in

advance of activity. Eating carbohydrates before the start of exercise is one of the more commonly used strategies to reduce the risk of hypoglycemia (26).

The type and amount of carbohydrates consumed before, during, and after exercise should be tailored to the specific activity. Generally, in situations involving a high level of circulating insulin,  $\sim$ 0.5–I.O g/kg/hour carbohydrate is required during exercise to maintain glycemia (26); however, if >2 hours have passed since the last prandial insulin dose,  $\sim$ 0.3–0.5 g/kg/hour is recommended (27,28). For prolonged or extended exercise (lasting  $\geq$ 2 hours), specific recommendations regarding how people with type I diabetes who use AID should tailor their carbohydrate intake for exercise are precluded because of a lack of evidence.

AID systems work to increase TIR and thereby lower overall mean glucose concentrations. Therefore, with an overall lower glucose target day-to-day, there may be an increased risk of hypoglycemia during exercise if no changes are made to prepare for exercise (29). With a lower starting glucose level, it is imperative that some of the previously discussed strategies (e.g., increasing the exercise glucose target to decrease IOB and/or reducing mealtime bolus insulin) are considered before exercise. Clinical exercise guidelines typically recommend a safe starting place for exercise of ~126–180 mg/dL (12,13). However, if no adjustments are made to the AID system and the pre-exercise glucose level is below this target range for activity, additional carbohydrate feeding is recommended.

## Practical Tips for Hypoglycemia Treatment With Exercise and AID

It is important to differentiate hypoglycemia *prevention* strategies for exercise from hypoglycemia *treatment* strategies for exercise with AID systems. Specifically, lower carbohydrate intake is often suggested for hypoglycemia treatment in those who use AID technology. This is because the AID algorithms anticipate hypoglycemia and cut back insulin delivery preemptively. The exact amount of carbohydrate (in grams) that should be recommended to treat hypoglycemia during exercise with AID technology is still unclear and requires controlled research studies for optimization of this strategy. How to best use this approach also depends on whether insulin delivery is being constrained during exercise by the AID system.

### Combination Strategies for AID and Exercise

Another option while using AID technology is to use a combination of setting a higher exercise target before exercise and reducing the mealtime bolus insulin to reduce the risk of exercise-associated hypoglycemia. A study by Tagougui et al. (27) found that a combination strategy of setting a higher exercise target and reducing mealtime bolus insulin by 33% in adults decreased the percentage of time spent in hypoglycemia (2.0 ± 6.2%) versus setting an exercise target alone (7.0 ± 12.6%) or setting no exercise target and using the full mealtime bolus (13.0 ± 19.0%). However, it is important to note that, in this study, the exercise occurred 90 minutes after the meal, which may have maximized the effect of a decreased mealtime insulin bolus with less IOB. If the exercise had occurred later (e.g., 3 hours after the meal), there may have been more IOB at the time of exercise commencement, as the reduced meal-time bolus would have resulted in a greater postprandial rise in glucose, which would have elicited an increase in insulin delivery by the AID system coinciding with the onset of exercise. Similarly, Myette-Côté et al. (30) recently found that, when exercise is initiated 60 or 120 minutes after a meal in adults with type I diabetes, the combination of a 33% meal bolus reduction and higher exercise target may be an effective and safe strategy to manage glycemia during 60 minutes of moderate-intensity aerobic exercise.

Another combination strategy involves setting an exercise target before exercise and consuming carbohydrates to reduce the risk of hypoglycemia during exercise. The exact amount of carbohydrate will vary depending on the type, intensity, and duration of exercise.

More research is needed to optimize these combination strategies and better understand the timing of exercise targets plus the timing and amount of carbohydrates necessary to maintain glycemia in the target range around exercise. McGaugh et al. (28) demonstrated in an open-loop pump study that a combined 50% basal rate reduction set at exercise onset and carbohydrate intake of 0.3 g/kg/hour was more effective than carbohydrate feeding alone during 2 hours of fasted walking. We have demonstrated in several recent studies that a combination of these recommended pre-exercise preparatory strategies using AID (exercise >3 hours after the meal, exercise target set 2 hours before exercise, and carbohydrate feeding with 15 g if blood glucose is <126 mg/dL 10 minutes before exercise) provides excellent glycemic stability during and after exercise (6,10).

#### Functional Issues With AID While Exercising

Functional challenges or issues that may occur with AID technology use during exercise include, but are not limited to, pump site failures, sensor failures/malfunctions, CGM sensors and infusion sets falling off because of increased perspiration, and CGM lag time leading to potentially dangerous failure to

detect dysglycemia (29,31–34). For example, individuals with type I diabetes who are involved in contact sports may experience an increased risk of potential trauma to the pump site or kinking/bending of the pump cannula. Additionally, sports and physical activity generally increase perspiration and may cause infusion sets, patch pumps, or sensors to lose their adhesive traction to the skin and, in some instances, fall off entirely.

Additional important considerations to avoid issues with AID use during exercise include the timing of infusion set changes and rotation, and timing of sensor changes. Each infusion set will have manufacturer recommendations on site change frequency and site rotations. Regularly changing infusion sites and following recommendations about site rotation are crucial to ensuring proper insulin delivery with AID systems. If site changes are delayed or infusion sites are not rotated regularly on the body, there is an increased risk of lipohypertrophy and/or scar tissue formation, which could cause the AID system to increase insulin infusion to prevent hyperglycemia and thereby result in excess insulin delivery, increasing the risk of hypoglycemia (35).

Certain water sports (e.g., swimming, surfing, and white-water rafting) and contact sports (e.g., tae kwon do, jiujitsu, judo, mixed martial arts, and football) may require different strategies for AID system use. For example, some individuals with type I diabetes may prefer to disconnect their insulin pump, when possible, during sports or exercise. The Omnipod 5 system is unique because the pump is a tubeless pod worn on the body, cannot be disconnected, and continues to function during activities (e.g., contact sports and swimming). In the water, the Bluetooth connection from the sensor to the pump may be lost, so the system will generally function using its Limited Mode of insulin delivery (36). In general, to reduce the risk of hypoglycemia during activity, pump suspension may not be as effective as setting a higher exercise target at least I-2 hours before the onset of exercise (24). Prolonged (>120 minutes) pump suspension in younger children (4-9 years of age) (37) may lead to elevated blood ketone levels, although this effect is rare (38), and may also increase the likelihood of forgetting to resume insulin delivery after exercise.

## Practical Tips to Avoid Functional Issues With AID During Exercise

Various overlay tapes and liquid adhesives are available online and in select stores and can be used to help keep infusion sets, patch pumps, and sensors adhered to the skin during exercise (33,39). If patients notice communication errors or issues with their sensor or pump use during exercise, one consideration is to choose an overlay tape that has an opening or cutout for the sensor or patch pump. This option may decrease the amount of perspiration build-up under the overlay tape, which could cause interference or affect device accuracy and/or communication.

Another practical consideration for people with type I diabetes who are involved in contact sports is to change and rotate infusion sites frequently to ensure appropriate insulin delivery with AID systems.

An important consideration regarding CGM lag time and rapid changes in glucose (e.g., a rapid decrease during aerobic exercise) is to avoid sensor calibrations during exercise. Because many CGM systems (i.e., the Dexcom G6 and G7 and the FreeStyle Libre 2 and 3) are currently factory-calibrated and do not require user calibrations, users who choose to calibrate should do so at a time that generally has less IOB, no food or exercise affecting glycemia, and a flat trend arrow (e.g., first thing in the morning). An additional strategy when individuals with type I diabetes are exercising and notice downward glycemic trend arrows or experience symptomatic responses to hypoglycemia is to perform a fingerstick blood glucose measurement and be prepared to supplement with carbohydrates earlier (i.e., in preparation for the potential sensor lag time that may not always capture hypoglycemia when blood glucose levels are changing rapidly) (40).

As previously noted, with the Omnipod 5 system, there is no option to disconnect the pump from the body during activity. This factor can be beneficial for individuals involved in water-based sports who may be concerned about prolonged pump disconnection and the risk of rebound hyperglycemia. However, for individuals using detachable pumps with tubing during activities (e.g., contact sports and some water-based activities), it is important to suspend (i.e., temporarily stop) insulin delivery. Not taking this step could cause problems. If, for example, glucose levels are above the target range, no exercise target was set before exercise, and the pump was simply disconnected from the body for exercise, the AID system may automatically deliver insulin while the pump is disconnected from the body, causing falsely increased IOB calculations and changing the algorithm decisions once the pump is reconnected after exercise.

#### Important Subgroups for AID and Exercise

In individuals with type I diabetes and impaired awareness of hypoglycemia (IAH), the ability to detect hypoglycemia symptoms is diminished or, in some cases, absent (4I,42), and this reduces their ability to take remedial action to prevent hypoglycemia. IAH results in a sixfold increase in the risk of severe hypoglycemia, and, given that  $\sim$ 20% of people with type I diabetes report having IAH (4I), there is a need to identify and manage this condition in the context of exercise and AID.

Although the methods for preventing hypoglycemia during exercise while using AID are the same for those with or without IAH (i.e., limiting insulin during/after exercise and supplementing with carbohydrates), greater vigilance around monitoring sensor and blood glucose levels is required for those experiencing IAH during exercise.

Children <6 years of age present unique challenges. They have rapid rates of glucose change, may not recognize or verbalize hypoglycemia symptoms, have unpredictable activity levels, and are sensitive to small doses of insulin. In an unpublished AID study involving supervised exercise, we observed a 5-year-old child have a decrease in sensor glucose from 163 to 88 mg/dL in 5 minutes, a rate of change of 15 mg/dL per minute, at which time the blood glucose was 36 mg/dL, and the child was unable to stand or talk (B.A.B., unpublished observations). In recent years, with more research focusing on very young children with type I diabetes who use AID systems, a greater emphasis on the impact of exercise on glycemia in this cohort is warranted.

#### Practical Tips for Subgroups Using AID Around Exercise

In a clinical context, it is important to understand if people with type I diabetes are experiencing IAH. Questionnaires (43,44) have been developed to classify a person's degree of awareness of hypoglycemia symptoms. Questionnaires developed by Gold et al. (43) and Clarke et al. (44) are commonly used, and a score ≥4 on either one indicates a degree of IAH. However, it is important to acknowledge that IAH is not an all-or-none phenomenon, but rather reflects a continuum along which differing degrees of impaired awareness can occur. For individuals in whom IAH is detected, in addition to following the above recommendations for managing hypoglycemia during exercise with AID, it is important to provide psychoeducation aimed at ensuring that their carbohydrate counting is accurate (to minimize inaccurate meal bolusing) and to maximize their ability to recognize hypoglycemia within their current limitations of IAH.

Helpful actions for very young children using AID systems are to set higher glucose targets before the exercise (which unfortunately cannot always be predicted) and have a knowledgeable adult present when a child who is prone to rapid exercise-induced glucose changes is engaging in exercise.

#### Summary and Future Directions for AID and Exercise

As insulin formulations, exercise and meal detection algorithms, and sensor technology continue to improve, we expect to see instrumental changes in the field of AID research and exercise for individuals with type I diabetes. It seems

likely that commercial AID manufacturers will need to catch up with open-source algorithms with regard to user-controlled alterations in aggressiveness. Additional areas of research that may significantly affect AID functionality in the future include dual-hormone (e.g., insulin and glucagon or insulin and pramlintide) AID therapy and additional signal inputs (e.g., continuous lactate, ketone, and/or insulin sensors, accelerometry, and galvanic skin temperature [6]).

AID technology continues to evolve and improve overall TIR while decreasing time below range for individuals with type I diabetes; however, there are many differences among the commercially available AID systems. This article has highlighted practical approaches to using AID to improve glycemic management around exercise. More research is needed to determine optimal strategies that can help all individuals with type I diabetes engage in safe exercise.

#### **DUALITY OF INTEREST**

D.P.Z. has received honoraria for speaking engagements from Ascensia Diabetes, Insulet Canada, and Medtronic Diabetes; is on an advisory board for Dexcom; and has received an ISPAD-JDRF Research Fellowship and research support from Insulet and the Leona M. and Harry B. Helmsley Charitable Trust. B.P. has received speaker honoraria fees from Medtronic. R.A.L. has received personal fees from Abbott Diabetes Care, Bioling, Capillary Biomedical, Deep Valley Laboratories, Gluroo, Provention Bio, and Tidepool. His work is supported by a Diabetes, Endocrinology and Metabolism Career Development grant (1K23DK122017) from the National Institute of Diabetes and Digestive and Kidney Diseases. He co-leads the Bioengineering and Behavioral Sciences Working Group of the Stanford Diabetes Research Center (P30 DK116074), and he has received additional research support from Insulet, JDRF, and Medtronic. B.A.B. serves on the advisory boards of Arecor, Medtronic, and Novo Nordisk; has received speaking fees from Eli Lilly; and has received research grant support from Insulet, Medtronic, and Tandem. D.N.O. has served on advisory boards for Abbott Laboratories, Medtronic, Merck Sharp & Dohme, Novo Nordisk, Roche, and Sanofi. He has received research support from Eli Lilly, Medtronic, Novo Nordisk, Roche, and Sanofi and travel support from Merck Sharp & Dohme and Novo Nordisk. No other potential conflicts of interest relevant to this article were reported.

#### **AUTHOR CONTRIBUTIONS**

D.P.Z. planned the manuscript outline and wrote the initial manuscript. D.M., B.P., R.A.L., B.A.B., and D.N.O. reviewed and edited the manuscript and approved the final version for submission. D.P.Z. is the guarantor of this work and, as such, takes responsibility for the integrity and accuracy of the contents.

#### REFERENCES

- Eckstein ML, Weilguni B, Tauschmann M, et al. Time in range for closed-loop systems versus standard of care during physical exercise in people with type 1 diabetes: a systematic review and meta-analysis. J Clin Med 2021;10:2445
- Brown SA, Kovatchev BP, Raghinaru D, et al.; iDCL Trial Research Group. Six-month randomized, multicenter trial of closed-loop control in type 1 diabetes. N Engl J Med 2019; 381:1707–1717

- Breton MD, Kanapka LG, Beck RW, et al.; iDCL Trial Research Group. A randomized trial of closed-loop control in children with type 1 diabetes. N Engl J Med 2020;383:836–845
- 4. Ware J, Allen JM, Boughton CK, et al.; KidsAP Consortium. Randomized trial of closed-loop control in very young children with type 1 diabetes. N Engl J Med 2022;386:209–219
- Mallad A, Hinshaw L, Schiavon M, et al. Exercise effects on postprandial glucose metabolism in type 1 diabetes: a tripletracer approach. Am J Physiol Endocrinol Metab 2015;308:E1106–E1115
- Paldus B, Morrison D, Zaharieva DP, et al. A randomized crossover trial comparing glucose control during moderateintensity, high-intensity, and resistance exercise with hybrid closed-loop insulin delivery while profiling potential additional signals in adults with type 1 diabetes. Diabetes Care 2022; 45:194–203
- McAuley SA, Horsburgh JC, Ward GM, et al. Insulin pump basal adjustment for exercise in type 1 diabetes: a randomised crossover study. Diabetologia 2016;59:1636–1644
- Guerci B, Sauvanet JP. Subcutaneous insulin: pharmacokinetic variability and glycemic variability. Diabetes Metab 2005;31: 4S7–4S24
- Heise T, Zijlstra E, Nosek L, Rikte T, Haahr H. Pharmacological properties of faster-acting insulin aspart vs insulin aspart in patients with type 1 diabetes receiving continuous subcutaneous insulin infusion: a randomized, double-blind, crossover trial. Diabetes Obes Metab 2017;19:208–215
- Morrison D, Zaharieva DP, Lee MH, et al. Comparable glucose control with fast-acting insulin aspart versus insulin aspart using a second-generation hybrid closed-loop system during exercise. Diabetes Technol Ther 2022;24:93–101
- 11. Phillip M, Nimri R, Bergenstal RM, et al. Consensus recommendations for the use of automated insulin delivery (AID) technologies in clinical practice. Endocr Rev. Online ahead of print on 6 September 2022 (doi: 10.1210/endrev/bnac022)
- 12. Riddell MC, Gallen IW, Smart CE, et al. Exercise management in type 1 diabetes: a consensus statement. Lancet Diabetes Endocrinol 2017;5:377–390
- Adolfsson P, Taplin CE, Zaharieva DP, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Exercise in children and adolescents with diabetes. Pediatr Diabetes 2022;23: 1341–1372
- 14. Maran A, Pavan P, Bonsembiante B, et al. Continuous glucose monitoring reveals delayed nocturnal hypoglycemia after intermittent high-intensity exercise in nontrained patients with type 1 diabetes. Diabetes Technol Ther 2010;12:763–768
- 15. Taplin CE, Cobry E, Messer L, McFann K, Chase HP, Fiallo-Scharer R. Preventing post-exercise nocturnal hypoglycemia in children with type 1 diabetes. J Pediatr 2010;157:784–8.e1
- Zaharieva DP, Messer L, Paldus B, O'Neal DN, Maahs D, Riddell MC. Glucose control during physical activity and exercise using closed loop technology in adults and adolescents with type 1 diabetes. Can J Diabetes 2020;44:740–749
- 17. Borg G. *Borg's Perceived Exertion and Pain Scales*. Champaign, IL, Human Kinetics, 1998
- 18. Rosales W, Cofré C, Alejandra C, et al. Validation of the Borg scale in participants with type 2 diabetes mellitus. Rev Med Chil 2016;144:1159–1163 [in Spanish]
- 19. Kendrick KR, Baxi SC, Smith RM. Usefulness of the modified 0–10 Borg scale in assessing the degree of dyspnea in patients with COPD and asthma. J Emerg Nurs 2000;26:216–222
- 20. Braune K, Lal RA, Petruželková L, et al.; OPEN International Healthcare Professional Network and OPEN Legal Advisory

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- Group. Open-source automated insulin delivery: international consensus statement and practical guidance for health-care professionals. Lancet Diabetes Endocrinol 2022;10:58–74
- Rabasa-Lhoret R, Bourque J, Ducros F, Chiasson JL. Guidelines for premeal insulin dose reduction for postprandial exercise of different intensities and durations in type 1 diabetic subjects treated intensively with a basal-bolus insulin regimen (ultralente-lispro). Diabetes Care 2001;24:625–630
- McMahon SK, Ferreira LD, Ratnam N, et al. Glucose requirements to maintain euglycemia after moderate-intensity afternoon exercise in adolescents with type 1 diabetes are increased in a biphasic manner. J Clin Endocrinol Metab 2007;92:963–968
- Morrison D, Paldus B, Zaharieva DP, et al. Late afternoon vigorous exercise increases postmeal but not overnight hypoglycemia in adults with type 1 diabetes managed with automated insulin delivery. Diabetes Technol Ther 2022;24:873–880
- 24. Zaharieva DP, McGaugh S, Pooni R, Vienneau T, Ly T, Riddell MC. Improved open-loop glucose control with basal insulin reduction 90 minutes before aerobic exercise in patients with type 1 diabetes on continuous subcutaneous insulin infusion. Diabetes Care 2019;42:824–831
- Tagougui S, Legault L, Heyman E, et al. Anticipated basal insulin reduction to prevent exercise-induced hypoglycemia in adults and adolescents living with type 1 diabetes. Diabetes Technol Ther 2022;24:307–315
- 26. Prévost MS, Rabasa-Lhoret R, Talbo MK, Yardley JE, Curry EG, Brazeau AS. Gender differences in strategies to prevent physical activity-related hypoglycemia in patients with type 1 diabetes: a better study. Diabetes Care 2022;45:e51–e53
- 27. Tagougui S, Taleb N, Legault L, et al. A single-blind, randomised, crossover study to reduce hypoglycaemia risk during postprandial exercise with closed-loop insulin delivery in adults with type 1 diabetes: announced (with or without bolus reduction) vs unannounced exercise strategies. Diabetologia 2020;63:2282–2291
- McGaugh SM, Zaharieva DP, Pooni R, et al. Carbohydrate requirements for prolonged, fasted exercise with and without basal rate reductions in adults with type 1 diabetes on continuous subcutaneous insulin infusion. Diabetes Care 2021;44:610–613
- Li A, Riddell MC, Potashner D, Brown RE, Aronson R. Time lag and accuracy of continuous glucose monitoring during high intensity interval training in adults with type 1 diabetes. Diabetes Technol Ther 2019;21:286–294
- 30. Myette-Côté E, Molveau J, Wu Z, et al. A randomized crossover pilot study evaluating glucose control during exercise initiated 1 or 2 h after a meal in adults with type 1 diabetes treated with an automated insulin delivery system. Diabetes Technol Ther. Online ahead of print 6 December 2022 (doi: 10.1089/dia. 2022.0338)
- 31. Zaharieva DP, Turksoy K, McGaugh SM, et al. Lag time remains with newer real-time continuous glucose monitoring technology during aerobic exercise in adults living with type 1 diabetes. Diabetes Technol Ther 2019;21:313–321

- 32. Englert K, Ruedy K, Coffey J, Caswell K, Steffen A; Diabetes Research in Children (DirecNet) Study Group. Skin and adhesive issues with continuous glucose monitors: a sticky situation. J Diabetes Sci Technol 2014;8:745–751
- 33. Messer LH, Berget C, Beatson C, Polsky S, Forlenza GP. Preserving skin integrity with chronic device use in diabetes. Diabetes Technol Ther 2018;20(Suppl. 2):S254–S264
- Messer LH, Tanenbaum ML, Cook PF, et al. Cost, hassle, and on-body experience: barriers to diabetes device use in adolescents and potential intervention targets. Diabetes Technol Ther 2020;22:760–767
- Heinemann L, Hirsch L, Hovorka R. Lipohypertrophy and the artificial pancreas: is this an issue? J Diabetes Sci Technol 2014;8:915–917
- 36. Hughes MS, Kingman RS, Hsu L, Lal RA, Buckingham BA, Zaharieva DP. Swimming with hybrid closed-loop: connectivity data from seven swimmers in the Omnipod 5 trial [Abstract]. Diabetes 2022;71(Suppl. 1):782-P
- 37. Wadwa RP, Chase HP, Raghinaru D, et al.; In Home Closed Loop Study Group. Ketone production in children with type 1 diabetes, ages 4–14 years, with and without nocturnal insulin pump suspension. Pediatr Diabetes 2017;18:422–427
- 38. Beck RW, Raghinaru D, Wadwa RP, Chase HP, Maahs DM; In Home Closed Loop Study Group. Frequency of morning ketosis after overnight insulin suspension using an automated nocturnal predictive low glucose suspend system. Diabetes Care 2014;37:1224–1229
- Litchman ML, Wawrzynski SE, Woodruff WS, Arrington JB, Nguyen QC, Gee PM. Continuous glucose monitoring in the real world using photosurveillance of #dexcom on Instagram: exploratory mixed methods study. JMIR Public Health Surveill 2019;5:e11024
- 40. Moser O, Riddell MC, Eckstein ML, et al. Glucose management for exercise using continuous glucose monitoring (CGM) and intermittently scanned CGM (isCGM) systems in type 1 diabetes: position statement of the European Association for the Study of Diabetes (EASD) and of the International Society for Pediatric and Adolescent Diabetes (ISPAD) endorsed by JDRF and supported by the American Diabetes Association (ADA). Diabetologia 2020;63:2501–2520
- Geddes J, Schopman JE, Zammitt NN, Frier BM. Prevalence of impaired awareness of hypoglycaemia in adults with type 1 diabetes. Diabet Med 2008;25:501–504
- 42. Lee MH, Vogrin S, Paldus B, et al. Glucose and counterregulatory responses to exercise in adults with type 1 diabetes and impaired awareness of hypoglycemia using closed-loop insulin delivery: a randomized crossover study. Diabetes Care 2020;43:480–483
- 43. Gold AE, MacLeod KM, Frier BM. Frequency of severe hypoglycemia in patients with type I diabetes with impaired awareness of hypoglycemia. Diabetes Care 1994;17:697–703
- 44. Clarke WL, Cox DJ, Gonder-Frederick LA, Julian D, Schlundt D, Polonsky W. Reduced awareness of hypoglycemia in adults with IDDM: a prospective study of hypoglycemic frequency and associated symptoms. Diabetes Care 1995;18:517–522

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